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10/558,276	11/18/2005	Thomas Wisniewski	05986/100M536-US1	3691

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EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/558,276	WISNIEWSKI ET AL.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,9-13,15-20,22,23,28-31,33-37,40,45,46 and 51-55* is/are pending in the application.

4a) Of the above claim(s) *11-13,15-19,29-31,33-37 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,9,10,20,22,23,28,45,46 and 51-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed June 30, 2009 in response to the Office Action of March 31, 2009 is acknowledged and has been entered. New claims 51-55 have been added. Claims 1, 9, 20 and 28 have been amended. Claims 11-13, 15-19, 29-31, 33-37 and 40 are withdrawn. Claims 1, 3, 9, 10, 20, 22, 23, 28, 45, 46 and 51-55 are under examination in this Office Action.

Claim Rejections - 35 USC § 112

Rejection of claim 28 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for Biological deposit **is withdrawn** upon further consideration.

New rejection in view of Applicant's amendment

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Rejection of Claims 1 under 35 U.S.C. 102(e) as being anticipated by Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) present in the Office action of 12/28/2007 **is reinstated** in view of Applicant's amendment. **New claim 54 is under 35 U.S.C. 102(e) as being anticipated by Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1).**

Applicant amended claim 1 to delete "the composition is suitable for mucosal administration". In the Final office action on 8/7/2008 the rejection under 35 U.S.C. 102(e) as being anticipated by Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) was withdrawn in view of Applicant's amendment adding the this limitation in claim 1 and a new rejection under under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) in view of Gizurarson et al. (US Patent 6,514,503 B1) was made. Because Applicant now amended the claims to delete this limitation the rejection under 35 U.S.C. 102(e) as being anticipated by Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) is reinstated.

Bachman et al. disclose a composition comprising a mammalian non-amyloidogenic prion protein, wherein the prion protein sequence is identical with the presently claimed SEQ ID NO: 4 and represents the elk prion protein (see SEQ ID NO: 82 of the sequence listing, and claims 1, 14, and 15). Bachman et al. disclose pharmaceutical and vaccine compositions comprising mammalian prion proteins formulated with an adjuvant aluminium hydroxide eliciting humoral immune response and alum as a pharmaceutically acceptable delivery vehicle (see [0035], [0080], and Example 15). While the intended use of the present composition is not limiting, it is noted that Bachman et al. disclose a vaccine and a pharmaceutical composition comprising prion proteins (see claims 44-57, [0003], [0021], [0027], [0079]).

Thus by this disclosure Bachman et al. anticipate the present claims.

Claim Rejections - 35 USC § 103

Rejection of Claims 1 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) in view of Gizurarson et al. (US Patent 6,514,503 B1) **is withdrawn** in view of Applicant's amendment. Claim 1 is now rejected under 35 U.S.C. 102(e) as being anticipated by Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claim 3 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) in view of Gizurarson et al. (US Patent 6,514,503 B1) and further in view of Peretz et al. (Nature 2001, Vol. 412, p. 739-743) and Kaneko et al. (JMB, 2000, Vol. 295, p. 997-1007) **is maintained.**

Rejection of Claim 4 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) and Gizurarson et al. (US Patent 6,514,503 B1) as applied to claim 1 and further in view of Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285, in IDS of 11/18/2005) **is maintained.**

Rejection of Claims 9 and 10 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Application Publication No.: 2003/0219459 A1) and Gizurarson et al. (US Patent 6,514,503 B1)as applied to claim 1 and further in view of Clemens et al. (US Patent 6,440,423 B1) and Kleanthous et al. (US Patent 6,585,975 B1) **is maintained.**

Rejection of Claims 20, 22 and 28 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) and further in view of Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) **is maintained.**

Rejection of Claims 23 and 46 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) as applied to claims 22 and further in view of Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285) **is maintained.**

Rejection of Claim 45 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) further in view of Peretz et al. (Nature 2001, Vol. 412, p. 739-743) and Kaneko et al. (JMB, 2000, Vol. 295, p. 997-1007) **is maintained.**

The rejection of claims 20, 22, 23, 28, 45, 46 is reiterated below, including new claims 51-53 and 55.

Claims 20, 22, 23, 28, 45-53 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760), Kotloff (Infection and Immunity, 2002, Vol. 70, p. 2016-2021) and further in view of Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) Lu et al. (US Patent 5,733,760)

Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285) Peretz et al. (Nature 2001, Vol. 412, p. 739-743) and Kaneko et al. (JMB, 2000, Vol. 295, p. 997-1007).

Amended claim 20 is construed to require either Shigella or Salmonella strain, as also acknowledged by Applicant in Remarks on page 19, third paragraph.

Bachman et al. and Gizurarson et al. teach composition comprising a mammalian prion protein formulated for mucosal administration as discussed above, wherein the prion protein sequence is identical with the presently claimed SEQ ID NO: 4 and represents the elk prion protein (see SEQ ID NO: 82 of the sequence listing, and claims 1, 14, and 15). Bachman's prion protein is comprised within the viral like particle and not the attenuated *Salmonella typhi* bacterium transfected spp strain as required by the present claims.

Lu et al. teach vaccine compositions comprising attenuated *Salmonella* vectors expressing heterologous DNA encoding viral antigens from HIV and HCV viruses (see the entire document, particularly claims 1-9, column 5, lines 65-67, column 10, lines 19-60). While Lu et al. teach *Salmonella typhi, Salmonella typhimurium, and Salmonella enteritidis*, (see column 6, lines 65-67, Lu et al. does not teach the specific *Salmonella* strains as recited in the present claim 28. **Kotloff** teaches attenuated *Shigella* strain (see the entire document).

Chabalgoity et al. teach *Salmonella typhimurium* LVR01 strain expressing heterologous antigens encoding binding fatty acid protein from *Echinococcus granulosus* (see the entire document, particularly Materials and Methods).

It would have been *prima facie* obvious to express mammalian prion protein in *Salmonella* bacterial vectors used for expression of heterologous antigens. Therefore it would have been obvious to provide a composition comprising attenuated *Salmonella typhi* bacterium

transfected spp strain transformed with a vector capable of expressing a mammalian prion protein.

One would have been motivated to substitute Lu's attenuated *Salmonella* vectors and Kotloffs *Shigella* strain for Bachman's viral particles and express mammalian prion proteins in *Salmonella* vectors because Lu et al. teach that their *Salmonella* vectors are particularly effective for induction of mucosal protective immune responses against mucosally transmitted infectious agents. Lu et al. also teach that attenuated Salmonella vectors are effective vectors for delivery of desired antigens because the bacteria grow rapidly and do not require growth in cell culture, thus allowing large scale production of vectors (see column 1, lines 19-55).

One would have been motivated to use Chabalgoity's *Salmonella typhimurium* LVR01 strain for expression of Bachman's prion proteins because Chabalgoity et al. teach that heterologous antigens expressed in LVR01 effectively elicits humoral and cellular immune responses in animals (see the entire document, particularly Results and Discussion on page 468).

One would have had a reasonable expectation of success to provide a composition comprising an attenuated *Salmonella typhi* bacterium and particularly *Salmonella typhimurium* LVR01 transformed with a vector capable of expressing a mammalian prion protein because the technology used for generation of bacterial recombinant vectors has been available to the skilled artisan at the time of the present invention. Moreover, the bacterial recombinant vectors expressing heterologous antigens have been successfully made in the art at the time of the invention as evidenced by Lu et al. and Chabalgoity et al.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 23 and 46 are drawn to a vaccine composition comprising an attenuated *Salmonella typhii* bacterium transfected spp strain transformed with a vector capable of expressing a mammalian prion protein, wherein all amino acids of the prion protein are D-amino acids.

Bachman et al. Gizurarson et al. and Lu et al. teach a vaccine composition comprising an attenuated *Salmonella typhii* bacterium transfected spp strain transformed with a vector capable of expressing a mammalian prion protein as discussed above.

Benkirane et al. teach that changing the amino acids within an antigenic peptide from an L-residue to the corresponding D-residue drastically increases the antigenicity of the peptide and contributes to the generation of high levels of IgG3 antibodies in immunized animals (see the entire document, particularly page 26279 and Discussion).

Thus based on the teaching of Benkirane et al., it would have been *prima facie* obvious to the person skilled in the art to provide a pharmaceutical composition designed for induction of immune responses, wherein the amino acids within the antigenic protein are D-amino acids.

One would have been motivated to provide Bachman's and Lu's pharmaceutical composition comprising attenuated *Salmonella typhii* transformed with a vector capable of expressing a mammalian prion protein wherein the amino acids of the prion protein are D-amino acids, because Benkirane et al. teach that changing the amino acids within an antigenic peptide from L- to D- amino acids results in increased antigenicity of the peptide.

One would have had a reasonable expectation of success to provide a composition comprising a mammalian prion protein wherein all amino acids are D-amino acids and to successfully use this composition for immunization purposes, because the means required for the

synthesis of proteins containing D-amino acid residues have been available to the skilled artisan at the time of the present invention as evidenced by Benkirane et al.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Bachman et al. and Gizurarson et al. teach a composition comprising a mammalian prion protein that is suitable for mucosal administration, as discussed above.

While Bachman teaches presently claimed SEQ ID NO: 4, Bachman does not teach specifically using residues 93-156 of SEQ ID NO: 4.

Peretz teaches that the region spanning amino acids 132-156 of an isolated prion protein is a critical determinant for inhibition of prion propagation by antibodies binding those particular amino acids (see page 741, right paragraph). **Kaneko** teaches that residues 90-144 of human prion protein are important for initiating prion disease (see Results and Table 1).

It would have been prima facie obvious and one would have been motivated to provide Bachman's prion composition consisting of residues 93-156 of the prion protein, because Peretz and Kaneko teach that residues 132-156 and 90-144 are critical for generation of neutralizing antibodies and are important for initiating prion disease. Thus since the prior art teaches that prion protein amino acid residues 90-156 contain the antibody epitopes and are critical for infection, the skilled artisan would have been motivated to provide presently claimed prion protein residues 93-156 for immunization purposes. Absent any unexpected results, it would have been obvious to use prion protein amino acid residues 93-156 for immunization purposes.

One would have had a reasonable expectation of success to provide prion composition for mucosal administration because the guidance for providing such compositions is available in the art.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicant's arguments

Applicant's arguments have been fully considered but fail to persuade. Applicant amended claim 1 to recite "A composition consisting essentially of". Applicant argues that "A skilled worker having read Bachmann would not have been led to arrive at the current claims because Bachmann teaches a composition comprising an isolated protein, alum, and a virus- like protein (hereafter "VLP"). The amended claims do not require a VLP. The VLP of the Bachmann composition is a critical element that improves the efficiency of vaccination by increasing the degree of repetitiveness of the antigen. See, Bachmann, paragraph [0012]. Furthermore, Bachmann discusses that a VLP is a core particle having a structure with an inherent organization that is bound to prion protein, dimers thereof, or prion peptides. See, Bachmann, paragraph [0014]. Additionally, Bachmann discloses that a prior protein is an antigen or antigenic determinant that interacts with a VLP to form an ordered and repetitive antigen array. See, Bachmann, paragraph [0015]." Applicant argues that the skilled worker after reading Bachmann would not have had an expectation of success to arrive at the compositions as required by the pending claims because he would have thought that a VLP is necessary to use a recombinant protein as an immunogen.

In response to Applicant's arguments it is the Office's position that the phrase "consisting essentially of" is construed as comprising. Thus, Bachman's composition comprising a VLP, a prion protein, an adjuvant and a delivery vehicle anticipates the present claims. It is also noted that Bachman's VLP acts as an adjuvant to the prion protein. Therefore, contrary to Applicants assertions, the skilled artisan would have had a reasonable expectation of success to arrive at the claimed composition because it is well known in the art that adjuvants, recited in present claim 1, aid in generation of immune responses to antigens. The skilled artisan would have expected that the VLP is not required in the composition comprising prion proteins and adjuvants, in order to generate an immune response in a subject. Thus, the skilled artisan would have expected that the present composition comprising a prion protein and an adjuvant would induce an immune response.

Applicant argues that "a skilled worker familiar with Gizurarson would also have been familiar with Czerkinsky; and, thus, the skilled worker would not have had a reasonable expectation of success for making a composition consisting essentially of an isolated non-amyloidogenic mammalian prion protein and consisting of one of an adjuvant and a delivery vehicle to elicit a humoral immune response that is associated with a mucosal IgA response with a composition containing a self-antigen. Instead, the same skilled worker would have expected that administration of a self-antigen would have resulted in immune tolerance. This would defeat the purpose of the claimed composition."

In response the Examiner notes that it has been well known in the art that administration of non-pathogenic prion protein antigens together with adjuvants results in generation of immune response as taught by Bachman (see claims 44-57, [0003], [0021], [0027], [0079]). Additionally,

the present claims are product claims and not method claims and the limitation "the composition elicits a humoral immune response" is viewed as intended use and is not considered limiting. The limitation "the composition is suitable for mucosal administration" has been deleted from claim 1 and thus claim 1 does not require that the present composition elicits mucosal immune responses or is formulated to be suitable for mucosal administration. Additionally, Applicant did not specify where the support for argued unexpected results (induction of immune responses with a non-amyloidogenic prion protein) can be found in the present specification.

Applicant's claims are drawn to compositions disclosed in the prior art as discussed in the rejections above. Applicant argues limitations that are not present in the claims. Thus in view of the foregoing the rejections are maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground of rejections presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/
Examiner, Art Unit 1648

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643